result in loss of user privileges and other penalties.

* * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 14:08:07 ON 04 JUN 2004

=> file .meeting
'EVENTLINE' IS NOT A VALID FILE NAME
Enter "HELP FILE NAMES" at an arrow prompt (=>) for a list of files
that are available. If you have requested multiple files, you can
specify a corrected file name or you can enter "IGNORE" to continue
accessing the remaining file names entered.
ENTER A FILE NAME OR (IGNORE):ignore

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'AGRICOLA' ENTERED AT 14:08:20 ON 04 JUN 2004

FILE 'BIOTECHNO' ENTERED AT 14:08:20 ON 04 JUN 2004

FILE 'CONFSCI' ENTERED AT 14:08:20 ON 04 JUN 2004

FILE 'HEALSAFE' ENTERED AT 14:08:20 ON 04 JUN 2004

FILE 'IMSDRUGCONF' ENTERED AT 14:08:20 ON 04 JUN 2004

FILE 'LIFESCI' ENTERED AT 14:08:20 ON 04 JUN 2004

FILE 'MEDICONF' ENTERED AT 14:08:20 ON 04 JUN 2004

FILE 'PASCAL' ENTERED AT 14:08:20 ON 04 JUN 2004

=> (sample size) and biomaker

L1	0	FILE AGRICOLA
L2	0	FILE BIOTECHNO
L3	0	FILE CONFSCI
L4	0	FILE HEALSAFE
L5	0	FILE IMSDRUGCONF
L6	0	FILE LIFESCI
L7	0	FILE MEDICONF
L8	0	FILE PASCAL

TOTAL FOR ALL FILES

L9	0	(SAMPLE SIZE) AND BIOMAKER

=> (sample size) and biomarker

L10	1	FILE AGRICOLA
L11	20	FILE BIOTECHNO
L12	0	FILE CONFSCI
L13	8	FILE HEALSAFE
L14	0	FILE IMSDRUGCONF

```
L15          20 FILE LIFESCI
L16           0 FILE MEDICONF
L17          30 FILE PASCAL

TOTAL FOR ALL FILES
L18          79 (SAMPLE SIZE) AND BIOMARKER

=> l18 and insulin
L19           0 FILE AGRICOLA
L20           0 FILE BIOTECHNO
L21           0 FILE CONFSCI
L22           0 FILE HEALSAFE
L23           0 FILE IMSDRUGCONF
L24           0 FILE LIFESCI
L25           0 FILE MEDICONF
L26           1 FILE PASCAL

TOTAL FOR ALL FILES
L27           1 L18 AND INSULIN

=> d l27 ibib abs total

L27   ANSWER 1 OF 1  PASCAL  COPYRIGHT 2004 INIST-CNRS. ALL RIGHTS RESERVED. on
      STN
ACCESSION NUMBER:         2002-0051671   PASCAL
COPYRIGHT NOTICE:         Copyright .COPYRGT. 2002 INIST-CNRS. All rights
                          reserved.
TITLE (IN ENGLISH):       Phase II randomized clinical trial of lycopene
                          supplementation before radical prostatectomy
AUTHOR:                   KUCUK Omer; SARKAR Fazlul H.; SAKR Wael; DJURIC Zora;
                          POLLAK Michael N.; KHACHIK Fred; LI Yi-Wei; BANERJEE
                          Mousumi; GRIGNON David; BERTRAM John S.; CRISSMAN John
                          D.; PONTES Edson J.; WOOD David P. JR
CORPORATE SOURCE:         Division of Hematology and Oncology, Wayne State
                          University, and Barbara Ann Karmanos Cancer Institute,
                          Detroit, MI, 48201, United States; Department of
                          Pathology, Wayne State University, and Barbara Ann
                          Karmanos Cancer Institute, Detroit, MI, 48201, United
                          States; Department of Medicine, McGill University and
                          Jewish General Hospital, Montreal, Quebec H3T 1E2,
                          Canada; Joint Institute for Applied Nutrition,
                          Department of Chemistry and Biochemistry, University
                          of Maryland, College Park, MD, 20742, United States;
                          Department of Biostatistics, Wayne State University,
                          and Barbara Ann Karmanos Cancer Institute, Detroit,
                          MI, 48201, United States; Cancer Research Center of
                          Hawaii, University of Hawaii, Honolulu, HI 96813,
                          United States; Department of Urology, Wayne State
                          University, and Barbara Ann Karmanos Cancer Institute,
                          Detroit, MI, 48201, United States
SOURCE:                   Cancer epidemiology, biomarkers & prevention, (2001),
                          10(8), 861-868, 72 refs.
                          ISSN: 1055-9965
DOCUMENT TYPE:            Journal
BIBLIOGRAPHIC LEVEL:      Analytic
COUNTRY:                  United States
LANGUAGE:                 English
AVAILABILITY:             INIST-26637, 354000099368250060
AN    2002-0051671   PASCAL
CP    Copyright .COPYRGT. 2002 INIST-CNRS. All rights reserved.
AB    An inverse association has been observed between dietary intake of
      lycopene and the risk of prostate cancer. We investigated the effects of
      lycopene supplementation in patients with prostate cancer. Twenty-six men
      with newly diagnosed, clinically localized (14 T.sub.1 and 12 T.sub.2)
```

prostate cancer were randomly assigned to receive 15 mg of lycopene (n = 15) twice daily or no supplementation (n = 11) for 3 weeks before radical prostatectomy. **Biomarkers** of differentiation and apoptosis were assessed by Western blot analysis on benign and malignant parts of the prostate gland. Prostatectomy specimens were entirely embedded, step-sectioned, and evaluated for pathological stage, Gleason score, volume of cancer, and extent of high-grade prostatic intraepithelial neoplasia. Plasma levels of lycopene, **insulin**-like growth factor-1 (IGF-1), IGF binding protein-3, and prostate-specific antigen were measured at baseline and after 3 weeks of supplementation or observation. Eleven (73%) subjects in the intervention group and two (18%) subjects in the control group had no involvement of surgical margins and/or extra-prostatic tissues with cancer (P = 0.02). Twelve (84%) subjects in the lycopene group and five (45%) subjects in the control group had tumors <4 ml in size (P = 0.22). Diffuse involvement of the prostate by high-grade prostatic intraepithelial neoplasia was present in 10 (67%) subjects in the intervention group and in 11 (100%) subjects in the control group (P = 0.05). Plasma prostate-specific antigen levels decreased by 18% in the intervention group, whereas they increased by 14% in the control group (P = 0.25). Expression of connexin 43 in cancerous prostate tissue was 0.63 ± 0.19 absorbance in the lycopene group compared with 0.25 ± 0.08 in the control group (P = 0.13). Expression of bcl-2 and bax did not differ significantly between the two study groups. IGF-1 levels decreased in both groups (P = 0.0002 and P = 0.0003, respectively). The results suggest that lycopene supplementation may decrease the growth of prostate cancer. However, no firm conclusions can be drawn at this time because of the small **sample size**.

```
=> l11 and l17
L28           1 FILE AGRICOLA
L29          20 FILE BIOTECHNO
L30           0 FILE CONFSCI
L31           8 FILE HEALSAFE
L32           0 FILE IMSDRUGCONF
L33          20 FILE LIFESCI
L34           0 FILE MEDICONF
L35          30 FILE PASCAL

TOTAL FOR ALL FILES
L36          79 L11 AND L17

=> l29 and py>1999
L37           0 FILE AGRICOLA
L38          11 FILE BIOTECHNO
'1999' NOT A VALID FIELD CODE
L39           0 FILE CONFSCI
L40           3 FILE HEALSAFE
L41           0 FILE IMSDRUGCONF
L42           9 FILE LIFESCI
'1999' NOT A VALID FIELD CODE
L43           0 FILE MEDICONF
L44          18 FILE PASCAL

TOTAL FOR ALL FILES
L45          41 L29 AND PY>1999

=> dup rem
ENTER L# LIST OR (END):l45
DUPLICATE IS NOT AVAILABLE IN 'IMSDRUGCONF, MEDICONF'.
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
PROCESSING COMPLETED FOR L45
L46           26 DUP REM L45 (15 DUPLICATES REMOVED)
```

=> d l46 ibib abs total

L46 ANSWER 1 OF 26 LIFESCI COPYRIGHT 2004 CSA on STN
ACCESSION NUMBER: 2004:24946 LIFESCI
TITLE: Statistical Analysis of Nonmonotonic Dose-Response Relationships: Research Design and Analysis of Nasal Cell Proliferation in Rats Exposed to Formaldehyde
AUTHOR: Gaylor, D.W.; Lutz, W.K.; Conolly, R.B.
CORPORATE SOURCE: Gaylor and Associates, Eureka Springs, Arkansas 72631
SOURCE: Toxicological Sciences [Toxicol. Sci.], (**20040100**) vol. 77, no. 1, pp. 158-164.
ISSN: 1096-6080.
DOCUMENT TYPE: Journal
FILE SEGMENT: X
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Statistical analyses of nonmonotonic dose-response curves are proposed, experimental designs to detect low-dose effects of J-shaped curves are suggested, and **sample sizes** are provided. For quantal data such as cancer incidence rates, much larger numbers of animals are required than for continuous data such as **biomarker** measurements. For example, 155 animals per dose group are required to have at least an 80% chance of detecting a decrease from a 20% incidence in controls to an incidence of 10% at a low dose. For a continuous measurement, only 14 animals per group are required to have at least an 80% chance of detecting a change of the mean by one standard deviation of the control group. Experimental designs based on three dose groups plus controls are discussed to detect nonmonotonicity or to estimate the zero equivalent dose (ZED), i.e., the dose that produces a response equal to the average response in the controls. Cell proliferation data in the nasal respiratory epithelium of rats exposed to formaldehyde by inhalation are used to illustrate the statistical procedures. Statistically significant departures from a monotonic dose response were obtained for time-weighted average labeling indices with an estimated ZED at a formaldehyde dose of 5.4 ppm, with a lower 95% confidence limit of 2.7 ppm. It is concluded that demonstration of a statistically significant bi-phasic dose-response curve, together with estimation of the resulting ZED, could serve as a point-of departure in establishing a reference dose for low-dose risk assessment.

L46 ANSWER 2 OF 26 LIFESCI COPYRIGHT 2004 CSA on STN DUPLICATE 1
ACCESSION NUMBER: 2003:89012 LIFESCI
TITLE: Prognostic Significance of Expression of p53 Oncoprotein in Primary (Stage I-IIIa) Non-Small Cell Lung Cancer
AUTHOR: Tan, D.-F.; Li, Q.; Rammath, N.; Beck, A.; Wiseman, S.; Anderson, T.; Al-Salameh, A.; Brooks, J.; Bepler, G.
CORPORATE SOURCE: Departments of Pathology and Cancer Genetics, Roswell Park Cancer Institute, Elm and Carlton Streets, Buffalo, New York 14263, USA; E-mail: dongfeng.tan@roswellpark.org
SOURCE: Anticancer Research [Anticancer Res.], (**20030400**) vol. 23, no. 2C, pp. 1665-1672.
ISSN: 0250-7005.
DOCUMENT TYPE: Journal
FILE SEGMENT: B
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Mutation of the p53 gene is one of the most common genetic abnormalities found in all types of human cancer. Accumulating evidence strongly indicates that p53 alterations play a role in tumorgenesis in non-small cell lung cancer (NSCLC). However, the role of p53 as a prognostic marker in NSCLC remains unclear. The data derived from the literature on prognostic impact of p53 in NSCLC has been a matter of controversy. Among the reasons for the discrepancy, are lack of correlation with key clinical

parameters, patients with different stages, different antibodies used, and insufficient **sample size**. The intent of this study was to evaluate the prognostic value of p53 protein in a larger cohort of stage I-IIIa patients. Clinicopathological data was obtained on 179 patients with NSCLC. These data were correlated with the p53 status on the respective surgically resected tumors, using monoclonal antibody DO7. There is a significant relationship between strong p53 expression and patient survival. In a multivariate analysis, strong expression (> 50%) of the p53 oncoprotein is an independently favorable prognostic factor. Patients with strong p53 expression had a prolonged survival (p = 0.009, RR; 0.56, 95% CI: 0.35-0.86). The median time of survival for patients with strong and negative/weak p53 expression was more than 61 and 44 months, respectively. The present study suggests that p53 protein expression in tumor tissue may serve as a prognostic **biomarker** for NSCLC. This information may also potentially serve as a tool for clinical decision-making when selecting patients for adjuvant treatments of NSCLC.

L46 ANSWER 3 OF 26 LIFESCI COPYRIGHT 2004 CSA on STN
ACCESSION NUMBER: 2004:26059 LIFESCI
TITLE: Semen Quality in Relation to **Biomarkers** of Pesticide Exposure
AUTHOR: Swan, S.H.; Kruse, R.L.; Liu, F.; Barr, D.B.; Drobnis, E.Z.; Redmon, J.B.; Wang, C.; Brazil, C.; Overstreet, J.W.
CORPORATE SOURCE: Department of Family and Community Medicine, MA306 Medical Sciences Building, University of Missouri-Columbia, Columbia, MO 65212 USA; E-mail: swans@health.missouri.edu
SOURCE: Environmental Health Perspectives [Environ. Health Perspect.], (**20030900**) vol. 111, no. 12, pp. 1478-1484.
ISSN: 0091-6765.
DOCUMENT TYPE: Journal
FILE SEGMENT: X
LANGUAGE: English
SUMMARY LANGUAGE: English
AB We previously reported reduced sperm concentration and motility in fertile men in a U.S. agrarian area (Columbia, MO) relative to men from U.S. urban centers (Minneapolis, MN; Los Angeles, CA; New York, NY). In the present study we address the hypothesis that pesticides currently used in agriculture in the Midwest contributed to these differences in semen quality. We selected men in whom all semen parameters (concentration, percentage sperm with normal morphology, and percentage motile sperm) were low (cases) and men in whom all semen parameters were within normal limits (controls) within Missouri and Minnesota (**sample sizes** of 50 and 36, respectively) and measured metabolites of eight current-use pesticides in urine samples provided at the time of semen collection. All pesticide analyses were conducted blind with respect to center and case-control status. Pesticide metabolite levels were elevated in Missouri cases, compared with controls, for the herbicides alachlor and atrazine and for the insecticide diazinon [2-isopropoxy-4-methyl-pyrimidinol (IMPY)]; for Wilcoxon rank test, p = 0.0007, 0.012, and 0.0004 for alachlor, atrazine, and IMPY, respectively. Men from Missouri with high levels of alachlor or IMPY were significantly more likely to be cases than were men with low levels [odds ratios (ORs) = 30.0 and 16.7 for alachlor and IMPY, respectively], as were men with atrazine levels higher than the limit of detection (OR = 11.3). The herbicides 2,4-D (2,4-dichlorophenoxyacetic acid) and metolachlor were also associated with poor semen quality in some analyses, whereas acetochlor levels were lower in cases than in controls (p = 0.04). No significant associations were seen for any pesticides within Minnesota, where levels of agricultural pesticides were low, or for the insect repellant DEET (N,N-diethyl-m-toluamide) or the malathion metabolic malathion dicarboxylic acid. These associations between current-use pesticides and reduced semen quality suggest that agricultural chemicals may have contributed to the reduction

in semen quality in fertile men from mid-Missouri we reported previously.

L46 ANSWER 4 OF 26 PASCAL COPYRIGHT 2004 INIST-CNRS. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2004-0130451 PASCAL
COPYRIGHT NOTICE: Copyright .COPYRGT. 2004 INIST-CNRS. All rights reserved.
TITLE (IN ENGLISH): Dose equivalency evaluation of major corticosteroids: Pharmacokinetics and cell trafficking and cortisol dynamics
AUTHOR: MAGER Donald E.; LIN Sheren X.; BLUM Robert A.; LATES Christian D.; JUSKO William J.
CORPORATE SOURCE: Department of Pharmaceutical Sciences, School of Pharmacy and Pharmaceutical Sciences, University at Buffalo, State University of New York, Buffalo, New York, United States; Buffalo Clinical Research Center, Buffalo, New York, United States
SOURCE: Journal of clinical pharmacology, **(2003)**, 43(11), 1216-1227, 35 refs.
ISSN: 0091-2700 CODEN: JCPCBR
DOCUMENT TYPE: Journal
BIBLIOGRAPHIC LEVEL: Analytic
COUNTRY: United States
LANGUAGE: English
AVAILABILITY: INIST-10257, 354000113386300050
AN 2004-0130451 PASCAL
CP Copyright .COPYRGT. 2004 INIST-CNRS. All rights reserved.
AB The integrity of current corticosteroid dose equivalency tables, as assessed by mechanistic models for cell trafficking and cortisol dynamics, was investigated in this study. Single, presumably equivalent, doses of intravenous hydrocortisone, methylprednisolone, dexamethasone, and oral prednisolone were given to 5 white men, according to total body weight, in a 5-way crossover, placebo-controlled study. Pharmacodynamic (PD) response-time profiles for T helper cells, T suppressor cells, neutrophils, and adrenal suppression were evaluated by extended indirect response models. For adrenal suppression, prednisolone appears to be less potent than methylprednisolone or dexamethasone. A good correlation was found between the estimated in vivo EC.sub.5.sub.0 values and relative receptor affinity (equilibrium dissociation constants normalized to dexamethasone). Area under the effect curves of all PD responses was calculated using a linear-trapezoidal method. Although T helper cell trafficking and adrenal suppression achieved significant differences by repeated-measures ANOVA ($p = 0.014$ and 0.022), post hoc analysis using the Bonferroni method revealed no difference between treatments. Although limited by the use of single doses and a relatively small **sample size**, this study applies mechanistic models for several **biomarkers** showing that currently used dosing tables reflect reasonable dose equivalency relationships for four corticosteroids.

L46 ANSWER 5 OF 26 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN DUPLICATE
ACCESSION NUMBER: 2003:36417960 BIOTECHNO
TITLE: Group sequential methods and **sample size** savings in **biomarker**-disease association studies
AUTHOR: Aplenc R.; Zhao H.; Rebbeck T.R.; Propert K.J.
CORPORATE SOURCE: R. Aplenc, Ctr. for Clin. Epidemiol./Biostat., Blockley Hall, 423 Guardian Dr., Philadelphia, PA 19104-6021, United States.
E-mail: raplenc@cceb.med.upenn.edu
SOURCE: Genetics, **(01 MAR 2003)**, 163/3 (1215-1219), 12 reference(s)
CODEN: GENTAE ISSN: 0016-6731
DOCUMENT TYPE: Journal; Article

COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 2003:36417960 BIOTECHNO
AB Molecular epidemiological association studies use valuable biosamples and incur costs. Statistical methods for early genotyping termination may conserve biosamples and costs. Group sequential methods (GSM) allow early termination of studies on the basis of interim comparisons. Simulation studies evaluated the application of GSM using data from a case-control study of GST genotypes and prostate cancer. Group sequential boundaries (GSB) were defined in the EAST-2000 software and were evaluated for study termination when early evidence suggested that the null hypothesis of no association between genotype and disease was unlikely to be rejected. Early termination of GSTM1 genotyping, which demonstrated no association with prostate cancer, occurred in >90% of the simulated studies. On average, 36.4% of biosamples were saved from unnecessary genotyping. In contrast, for GSTT1, which demonstrated a positive association, inappropriate termination occurred in only 6.6%. GSM may provide significant cost and sample savings in molecular epidemiology studies.

L46 ANSWER 6 OF 26 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN DUPLICATE
ACCESSION NUMBER: 2003:36988123 BIOTECHNO
TITLE: Biological monitoring for selected herbicide **biomarkers** in the urine of exposed custom applicators: Application of mixed-effect models
AUTHOR: Hines C.J.; Deddens J.A.; Striley C.A.F.; Biagini R.E.; Shoemaker D.A.; Brown K.K.; MacKenzie B.A.; Hull R.D.
CORPORATE SOURCE: C.J. Hines, Natl. Inst. for Occup. Safety/Health, 4676 Columbia Pkwy, Cincinnati, OH 45226, United States. E-mail: chines@cdc.gov
SOURCE: Annals of Occupational Hygiene, (**2003**), 47/6 (503-517), 35 reference(s)
CODEN: AOHYA3 ISSN: 0003-4878
DOCUMENT TYPE: Journal; Article
COUNTRY: United Kingdom
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 2003:36988123 BIOTECHNO
AB Metabolites and/or parent compounds of the herbicides atrazine, alachlor, metolachlor, cyanazine and the 2-ethylhexyl ester of 2,4-dichlorophenoxyacetic acid (2,4-D) were measured in the urine of 15 custom applicators who each provided from five to seven 24 h urine samples during a 6 week period (n = 87). Each applicator provided a pre-season urine sample and a reference population (n = 46) provided first-morning urine samples. Urinary **biomarkers** were measured by either immunoassay or gas chromatography. During the spraying season, the geometric mean amount of alachlor mercapturate equivalents (eq.), atrazine eq., 2,4-D and metolachlor mercapturate eq. excreted in 24 h was 17, 19, 110 and 22 nmol, respectively. Mixed-effect models were used to determine predictors of the amount of atrazine eq. and 2,4-D excreted in 24 h. The specific days of herbicide spraying associated with increased **biomarker** excretion varied for the two analytes, and included one or more days prior to urine collection. This confirms the importance of collecting covariate information on day(s) most relevant to the **biomarker** of interest. The within-worker variance component, expressed as a geometric standard deviation (.sub.WGSD range: 2.5-2.9), was substantially larger than the between-worker component (.sub.BGSD range: 1.3-1.5) for the modeled **biomarkers**. Alachlor mercapturate eq. and metolachlor mercapturate eq. were detected in more than half of the applicator pre-season urine samples. All **biomarkers** were detected infrequently in the reference population. Evaluation of non-spray exposure determinants was limited by

inclusion of prior day spraying, adjustment for time and the small **sample size**.

L46 ANSWER 7 OF 26 PASCAL COPYRIGHT 2004 INIST-CNRS. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2003-0136913 PASCAL
COPYRIGHT NOTICE: Copyright .COPYRGT. 2003 INIST-CNRS. All rights reserved.
TITLE (IN ENGLISH): MRI as a **biomarker** of disease progression in a therapeutic trial of milameline for AD
AUTHOR: JACK C. R. JR; SLOMKOWSKI M.; GRACON S.; HOOVER T. M.; FELMLEE J. P.; STEWART K.; XU Y.; SHIUNG M.; O'BRIEN P. C.; CHA R.; KNOPMAN D.; PETERSEN R. C.
CORPORATE SOURCE: Department of Diagnostic Radiology, Mayo Clinic and Foundation, Rochester, MN, United States; Pharmaceutical Research, Parke-Davis (Pfizer), Ann Arbor, MI, United States; Department of Biostatistics, Mayo Clinic and Foundation, Rochester, MN, United States; Department of Neurology, Mayo Clinic and Foundation, Rochester, MN, United States
SOURCE: Neurology, **(2003)**, 60(2), 253-260, 24 refs. ISSN: 0028-3878 CODEN: NEURAI
DOCUMENT TYPE: Journal
BIBLIOGRAPHIC LEVEL: Analytic
COUNTRY: United States
LANGUAGE: English
AVAILABILITY: INIST-6345, 354000104041850180
AN 2003-0136913 PASCAL
CP Copyright .COPYRGT. 2003 INIST-CNRS. All rights reserved.
AB Objective: To assess the feasibility of using MRI measurements as a surrogate endpoint for disease progression in a therapeutic trial for AD. Methods: A total of 362 patients with probable AD from 38 different centers participated in the MRI portion of a 52-week randomized placebo-controlled trial of milameline, a muscarinic receptor agonist. The therapeutic trial itself was not completed due to projected lack of efficacy on interim analysis; however, the MRI arm of the study was continued. Of the 362 subjects who underwent a baseline MRI study, 192 subjects underwent a second MRI 1 year later. Hippocampal volume and temporal horn volume were measured from the MRI scans. Results: The annualized percent changes in hippocampal volume (-4.9%) and temporal horn volume (16.1%) in the study patients were consistent with data from prior single-site studies. Correlations between the rate of MRI volumetric change and change in behavioral/cognitive measures were greater for the temporal horn than for the hippocampus. Decline over time was more consistently seen with imaging measures, 99% of the time for the hippocampus, than behavioral/cognitive measures ($p < 0.001$). Greater consistency in MRI than behavioral/clinical measures resulted in markedly lower estimated **sample size** requirements for clinical trials. The estimated number of subjects per arm required to detect a 50% reduction in the rate of decline over 1 year are: AD Assessment Scale-cognitive subscale 320; Mini-Mental Status Examination 241; hippocampal volume 21; temporal horn volume 54. Conclusion: The consistency of MRI measurements obtained across sites, and the consistency between the multisite milameline data and that obtained in prior single-site studies, demonstrate the technical feasibility of using structural MRI measures as a surrogate endpoint of disease progression in therapeutic trials. However, validation of imaging as a **biomarker** of therapeutic efficacy in AD awaits a positive trial.

L46 ANSWER 8 OF 26 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
ACCESSION NUMBER: 2003:36764702 BIOTECHNO
TITLE: Urinary PAH metabolites influenced by genetic polymorphisms of GSTM1 in male hospital incinerator workers

AUTHOR: Lee K.-H.; Cho S.-H.; Hong Y.-C.; Lee K.-H.; Kwan H.-J.; Choi I.; Kang D.
CORPORATE SOURCE: D. Kang, Department of Preventive Medicine, Seoul Natl. Univ. Coll. of Medicine, Institute of Environmental Medicine, 28 Yongon-Dong Chongno-Gu, Seoul, 110-799, South Korea.
SOURCE: Journal of Occupational Health, (**2003**), 45/3 (168-171), 23 reference(s)
CODEN: JOCHFV ISSN: 1341-9145
DOCUMENT TYPE: Journal; Article
COUNTRY: Japan
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 2003:36764702 BIOTECHNO
AB Hospital waste incinerator workers are exposed to various pyrolysis products including polycyclic aromatic hydrocarbons (PAHs). We evaluated their exposure by assessing urinary 1-hydroxypyrene glucuronide (1-OHPG), as an internal dose of PAH exposure. The potential effect of genetic polymorphisms of GSTM1/T1 involved in PAH metabolisms was also investigated. Pre- and post-shift samples were collected from 28 hospital incinerator workers. Urinary 1-OHPG was assayed by synchronous fluorescence spectroscopy (SFS) after immunoaffinity purification with the monoclonal antibody 8E11. Genotypes of GSTM1/T1 were assessed by PCR-based methods. Information on smoking habits and use of personal protective equipment were collected by means of a self-administered questionnaire. The Mann-Whitney test was used to compare group means of these **biomarkers**. Urinary 1-OHPG levels were similar in pre- and post-shift urine samples. The arithmetic mean concentrations of urinary 1-OHPG were 0.16 ± 0.04 μmol/mol creatinine pre-shift and 0.19 ± 0.09 μmol/mol creatinine post-shift, but urinary 1-OHPG levels were significantly higher in individuals with the GSTM1 null genotype than with the GSTM1 present genotype ($p=0.05$, by Mann-Whitney test). Our results suggest that the urinary 1-OHPG levels in hospital waste incinerator workers may be modified by the GSTM1 genotype, but these findings remain to be confirmed in future studies involving larger **sample sizes**.

L46 ANSWER 9 OF 26 BIOTECHNO
ACCESSION NUMBER: 2003:36523116 BIOTECHNO
TITLE: Selecting differentially expressed genes from microarray experiments
AUTHOR: Pepe M.S.; Longton G.; Anderson G.L.; Schummer M.
CORPORATE SOURCE: M.S. Pepe, Department of Biostatistics, University of Washington, Seattle, WA 98195-7232, United States. E-mail: mspepe@u.washington.edu
SOURCE: Biometrics, (**2003**), 59/1 (133-142), 22 reference(s)
CODEN: BIOMA5 ISSN: 0006-341X
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English; French
AN 2003:36523116 BIOTECHNO
AB High throughput technologies, such as gene expression arrays and protein mass spectrometry, allow one to simultaneously evaluate thousands of potential **biomarkers** that could distinguish different tissue types. Of particular interest here is distinguishing between cancerous and normal organ tissues. We consider statistical methods to rank genes (or proteins) in regards to differential expression between tissues. Various statistical measures are considered, and we argue that two measures related to the Receiver Operating Characteristic Curve are particularly suitable for this purpose. We also propose that sampling variability in the gene rankings be quantified, and suggest using the "selection probability function," the probability distribution of

rankings for each gene. This is estimated via the bootstrap. A real dataset, derived from gene expression arrays of 23 normal and 30 ovarian cancer tissues, is analyzed. Simulation studies are also used to assess the relative performance of different statistical gene ranking measures and our quantification of sampling variability. Our approach leads naturally to a procedure for **sample-size** calculations, appropriate for exploratory studies that seek to identify differentially expressed genes.

L46 ANSWER 10 OF 26 PASCAL COPYRIGHT 2004 INIST-CNRS. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2003-0033386 PASCAL

TITLE (IN ENGLISH): Phase II clinical trial of N-(4-hydroxyphenyl)retinamide and tamoxifen administration before definitive surgery for breast neoplasia

AUTHOR: SINGLETARY S. Eva; ATKINSON Edward N.; HOQUE Ashraful; SNEIGE Nour; SAHIN Ayse A.; FRITSCHE Herbert A. JR; LOTAN Reuben; LU Tao; HITTELMAN Walter N.; BEVERS Therese B.; STELLING Carol B.; LIPPMAN Scott M.

CORPORATE SOURCE: Department of Surgical Oncology, Research Laboratory Medicine, Thoracic/Head and Neck Medical Oncology, Experimental Therapeutics, and Diagnostic Imaging, The University of Texas M. D. Anderson Cancer Center, Houston, Texas 77030, United States; Department of Biomathematics, Research Laboratory Medicine, Thoracic/Head and Neck Medical Oncology, Experimental Therapeutics, and Diagnostic Imaging, The University of Texas M. D. Anderson Cancer Center, Houston, Texas 77030, United States; Department of Clinical Cancer Prevention, Research Laboratory Medicine, Thoracic/Head and Neck Medical Oncology, Experimental Therapeutics, and Diagnostic Imaging, The University of Texas M. D. Anderson Cancer Center, Houston, Texas 77030, United States; Department of Pathology, The University of Texas M. D. Anderson Cancer Center, Houston, Texas 77030, United States; Department of Research Laboratory Medicine, The University of Texas M. D. Anderson Cancer Center, Houston, Texas 77030, United States; Department of Thoracic/Head and Neck Medical Oncology, The University of Texas M. D. Anderson Cancer Center, Houston, Texas 77030, United States; Department of Experimental Therapeutics, The University of Texas M. D. Anderson Cancer Center, Houston, Texas 77030, United States; Department of Diagnostic Imaging, The University of Texas M. D. Anderson Cancer Center, Houston, Texas 77030, United States

SOURCE: Clinical cancer research, **(2002)**, 8(9), 2835-2842, 48 refs.
ISSN: 1078-0432

DOCUMENT TYPE: Journal
BIBLIOGRAPHIC LEVEL: Analytic
COUNTRY: United States
LANGUAGE: English
AVAILABILITY: INIST-26073, 354000105065910100

AN 2003-0033386 PASCAL

AB Purpose: Surrogate end point **biomarkers** (SEBs) that can be measured in ductal carcinoma in situ or early-stage invasive cancer are needed to improve the efficiency and reduce the cost of chemoprevention trials. Experimental Design: We conducted a prospective study to develop SEBs for tamoxifen and N-[4-hydroxyphenyl]retinamide by administering

either a placebo or both drugs for 2-4 weeks to women with ductal carcinoma in situ or early invasive cancers in the interval between the initial diagnostic core biopsy and definitive surgery. The major statistical end point of the study was pre- versus posttreatment change in cell proliferation, as measured by changes in Ki67 labeling indices. In addition, estrogen receptor (ER), HER2/neu, p53, retinoid receptors, and DNA index were measured. Results: Between February 1997 and April 200, 52 patients were registered on the study, and 36 (20 in the placebo arm and 16 in the treatment arm) were available for analysis. No statistically significant pre- versus posttreatment differences in Ki67 labeling index or in the other markers were observed in the treatment arm compared with the placebo arm. There was a trend toward increased treatment response in ER-positive versus ER-negative patients, but this could not be rigorously analyzed because of the low **sample size** and the unequal distribution of ER-positive patients in the two study arms. Conclusion: Future SEB trials for breast carcinoma must (a) incorporate information about patient hormonal status into the study design and (b) resolve problems in patient accrual.

L46 ANSWER 11 OF 26 LIFESCI COPYRIGHT 2004 CSA on STN DUPLICATE 4
ACCESSION NUMBER: 2002:114806 LIFESCI
TITLE: C-tau **biomarker** of neuronal damage in severe brain injured patients: association with elevated intracranial pressure and clinical outcome
AUTHOR: Zemlan, F.P.*; Jauch, E.C.; Mulchahey, J.J.; Gabbita, S.P.; Rosenberg, W.S.; Speciale, S.G.; Zuccarello, M.
CORPORATE SOURCE: Department of Psychiatry, University of Cincinnati College of Medicine, Cincinnati, OH 45267-0559, USA; E-mail: zemlanf@email.uc.edu
SOURCE: Brain Research [Brain Res.], (**20020823**) vol. 947, no. 1, pp. 131-139.
ISSN: 0006-8993.
DOCUMENT TYPE: Journal
FILE SEGMENT: N3
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Following traumatic brain injury, the neuronally-localized intracellular protein MAP-tau is proteolytically cleaved (C-tau) and gains access to cerebrospinal fluid (CSF) and serum. The present study compared initial CSF C-tau levels, initial Glasgow Coma Scale (GCS) scores and elevated intracranial pressure (ICP) as predictors of clinical outcome. In this preliminary, prospective study of consecutive severe traumatic brain injured patients (TBI) clinical outcome was quantified with the Glasgow Outcome Scale (GOS) at discharge (n=28). Sensitivity and specificity of initial C-tau levels and initial GCS scores as predictors of clinical outcome is reported. To assess disease specificity C-tau levels were compared between TBI patients and neurologic (n=87) and non-neurologic control patients (n=67). Initial CSF C-tau levels were elevated 40,000 fold in TBI patients compared to either neurologic or non-neurologic control patients (P0.001). Initial C-tau levels were correlated with clinical outcome (P=0.006) and were a significant predictor of dichotomized clinical outcome (P=0.011) demonstrating a sensitivity of prediction of 92% and a specificity of 94%. Initial C-tau levels were also a significant predictor of subsequent ICP with higher initial C-tau levels associated with elevated ICP (P=0.014). Initial GCS score were correlated with clinical outcome (P=0.026) and demonstrated a sensitivity of 50% and a specificity of 100% for predicting dichotomized clinical outcome. Statistical analysis indicated that initial C-tau levels and initial GCS scores were independent predictors of clinical outcome. The present preliminary study demonstrates that initial CSF C-tau levels are a significant predictor of ICP and clinical outcome with particular sensitivity for identifying severe TBI patients with good clinical outcome. Future studies employing a larger **sample size** and clinical outcome assessment at longer periods after hospitalization

will be needed to determine the utility of initial C-tau levels as a clinical **biomarker** in TBI.

L46 ANSWER 12 OF 26 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
ACCESSION NUMBER: 2002:35137243 BIOTECHNO
TITLE: Detection of dermcidin-derived peptides in sweat by ProteinChip® technology
AUTHOR: Flad T.; Bogumil R.; Tolson J.; Schittek B.; Garbe C.; Deeg M.; Mueller C.A.; Kalbacher H.
CORPORATE SOURCE: T. Flad, Sect. for Transplantation Immunology, University of Tuebingen, Waldhoernlestr. 22, 72072 Tuebingen, Germany.
E-mail: thomas.flad@uni-tuebingen.de
SOURCE: Journal of Immunological Methods, **(01 DEC 2002)**, 270/1 (53-62), 18 reference(s)
CODEN: JIMMBG ISSN: 0022-1759
PUBLISHER ITEM IDENT.: S0022175902002296
DOCUMENT TYPE: Journal; Article
COUNTRY: Netherlands
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 2002:35137243 BIOTECHNO
AB Recently, a novel antimicrobial peptide DCD-1, derived from the Dermcidin (DCD) gene and secreted by sweat glands, has been described by Schittek et al. [Nat. Immunol. 2 (2001) 1133.]. Here we describe the application of the surface-enhanced laser desorption/ionisation (SELDI) technology for the detection of DCD-1 and other dermcidin-derived peptides directly from microlitre amounts of human sweat. The advantages of the technique are as follows: (a) it can be carried out with ease and rapidity; (b) multiple samples can be processed simultaneously; (c) prior purification is not required; and (d) only a limited sample volume is necessary for both protein profiling and semiquantitation. Profiling of human sweat from various donors revealed that in addition to DCD-1, other DCD-derived peptide species were also present in significant quantities. Four of five identified peptides were DCD-1 related, while the fifth corresponded to a portion of the DCD protein outside the DCD-1 core. This provides clues as to how the novel protein is processed to its active form, though further work remains to elucidate this fully. Thus, we have demonstrated the applicability of such technology to the detection of DCD-1 and for the protein profiling of sweat in general. Such studies could reveal valuable new **biomarkers** for diagnosis and treatment of skin and sweat gland disorders. .COPYRGT. 2002 Elsevier Science B.V. All rights reserved.

L46 ANSWER 13 OF 26 PASCAL COPYRIGHT 2004 INIST-CNRS. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2001-0461396 PASCAL
COPYRIGHT NOTICE: Copyright .COPYRGT. 2001 INIST-CNRS. All rights reserved.
TITLE (IN ENGLISH): Factors contributing to peak broadening and mass accuracy in the characterization of intact spores using matrix-assisted laser desorption/ionization coupled with time-of-flight mass spectrometry
AUTHOR: RAMIREZ Javier; FENSELAU Catherine
CORPORATE SOURCE: Department of Chemistry and Biochemistry, University of Maryland, College Park, MD 20742, United States
SOURCE: Journal of mass spectrometry, **(2001)**, 36(8), 929-936, 38 refs.
ISSN: 1076-5174
DOCUMENT TYPE: Journal
BIBLIOGRAPHIC LEVEL: Analytic
COUNTRY: United Kingdom
LANGUAGE: English
AVAILABILITY: INIST-22950, 354000096109900100

AN 2001-0461396 PASCAL
CP Copyright .COPYRGT. 2001 INIST-CNRS. All rights reserved.
AB Factors contributing to peak broadening, accuracy and precision in mass assignment in the matrix-assisted laser desorption/ionization characterization of a lipopeptide desorbed from intact Bacillus spores were investigated. These spores were studied as an example of a thick, topologically irregular sample, which present a more difficult target than a pure peptide or protein. The type of matrix, matrix:sample ratio, laser fluence, and localized repetitive laser irradiation were all found to affect the full-width at half maximum of the **biomarker**. Both in-source and post-source phenomena were shown to contribute. Sample thickness had less effect. Precision and accuracy of mass assignment were also affected by matrix:sample ratio and laser fluence. In general, this sample was responsive to the same experimental variables as pure peptides, and the use of an internal standard produced significant improvements in precision and accuracy.

L46 ANSWER 14 OF 26 PASCAL COPYRIGHT 2004 INIST-CNRS. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2001-0350491 PASCAL
COPYRIGHT NOTICE: Copyright .COPYRGT. 2001 INIST-CNRS. All rights reserved.
TITLE (IN ENGLISH): Time of flight secondary ion mass spectrometry (ToFSIMS) of a number of hopanoids
AUTHOR: STEELE A.; TOPORSKI J. K. W.; AVCI R.; GUIDRY S.; MCKAY D. S.
CORPORATE SOURCE: Astrobiology Group, University of Portsmouth, School of Earth Environmental and Physical Sciences, Burnaby Road, Portsmouth PO1 3QL, United Kingdom; Astrobiology Group, NASA, Johnson Space Centre, Houston, TX 77058, United States; ICAL, Department of Physics, Montana State University EPS 264, Bozeman, MT 59717, United States; University of Houston, Department of Geosciences, Houston, TX 77204-5503, United States
SOURCE: Organic geochemistry, **(2001)**, 32(7), 905-911, 29 refs.
Illustrations; Table
ISSN: 0146-6380
DOCUMENT TYPE: Journal
BIBLIOGRAPHIC LEVEL: Analytic
COUNTRY: United Kingdom
LANGUAGE: English
AVAILABILITY: INIST-17824, 354000098425360030
AN 2001-0350491 PASCAL
CP Copyright .COPYRGT. 2001 INIST-CNRS. All rights reserved.
AB Time of flight secondary ion mass spectrometry (ToFSIMS) has been applied to a number of bacterial hopanoids in an attempt to characterise these geologically important molecules in situ by a surface sensitive technique. Our results show that these molecules can be detected using this instrumentation to a high degree of mass accuracy. We believe that ToFSIMS can, therefore, be used to identify these molecules in environmental samples where **sample size** may be an issue and contraindicate the use of more traditional techniques such as GC-MS.

L46 ANSWER 15 OF 26 PASCAL COPYRIGHT 2004 INIST-CNRS. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2002-0051671 PASCAL
COPYRIGHT NOTICE: Copyright .COPYRGT. 2002 INIST-CNRS. All rights reserved.
TITLE (IN ENGLISH): Phase II randomized clinical trial of lycopene supplementation before radical prostatectomy
AUTHOR: KUCUK Omer; SARKAR Fazlul H.; SAKR Wael; DJURIC Zora; POLLAK Michael N.; KHACHIK Fred; LI Yi-Wei; BANERJEE

Mousumi; GRIGNON David; BERTRAM John S.; CRISSMAN John D.; PONTES Edson J.; WOOD David P. JR

CORPORATE SOURCE: Division of Hematology and Oncology, Wayne State University, and Barbara Ann Karmanos Cancer Institute, Detroit, MI, 48201, United States; Department of Pathology, Wayne State University, and Barbara Ann Karmanos Cancer Institute, Detroit, MI, 48201, United States; Department of Medicine, McGill University and Jewish General Hospital, Montreal, Quebec H3T 1E2, Canada; Joint Institute for Applied Nutrition, Department of Chemistry and Biochemistry, University of Maryland, College Park, MD, 20742, United States; Department of Biostatistics, Wayne State University, and Barbara Ann Karmanos Cancer Institute, Detroit, MI, 48201, United States; Cancer Research Center of Hawaii, University of Hawaii, Honolulu, HI 96813, United States; Department of Urology, Wayne State University, and Barbara Ann Karmanos Cancer Institute, Detroit, MI, 48201, United States

SOURCE: Cancer epidemiology, biomarkers & prevention, **(2001)**, 10(8), 861-868, 72 refs.
ISSN: 1055-9965

DOCUMENT TYPE: Journal
BIBLIOGRAPHIC LEVEL: Analytic
COUNTRY: United States
LANGUAGE: English
AVAILABILITY: INIST-26637, 354000099368250060
AN 2002-0051671 PASCAL

AB An inverse association has been observed between dietary intake of lycopene and the risk of prostate cancer. We investigated the effects of lycopene supplementation in patients with prostate cancer. Twenty-six men with newly diagnosed, clinically localized (14 T.sub.1 and 12 T.sub.2) prostate cancer were randomly assigned to receive 15 mg of lycopene (n = 15) twice daily or no supplementation (n = 11) for 3 weeks before radical prostatectomy. **Biomarkers** of differentiation and apoptosis were assessed by Western blot analysis on benign and malignant parts of the prostate gland. Prostatectomy specimens were entirely embedded, step-sectioned, and evaluated for pathological stage, Gleason score, volume of cancer, and extent of high-grade prostatic intraepithelial neoplasia. Plasma levels of lycopene, insulin-like growth factor-1 (IGF-1), IGF binding protein-3, and prostate-specific antigen were measured at baseline and after 3 weeks of supplementation or observation. Eleven (73%) subjects in the intervention group and two (18%) subjects in the control group had no involvement of surgical margins and/or extra-prostatic tissues with cancer (P = 0.02). Twelve (84%) subjects in the lycopene group and five (45%) subjects in the control group had tumors <4 ml in size (P = 0.22). Diffuse involvement of the prostate by high-grade prostatic intraepithelial neoplasia was present in 10 (67%) subjects in the intervention group and in 11 (100%) subjects in the control group (P = 0.05). Plasma prostate-specific antigen levels decreased by 18% in the intervention group, whereas they increased by 14% in the control group (P = 0.25). Expression of connexin 43 in cancerous prostate tissue was 0.63 ± 0.19 absorbance in the lycopene group compared with 0.25 ± 0.08 in the control group (P = 0.13). Expression of bcl-2 and bax did not differ significantly between the two study groups. IGF-1 levels decreased in both groups (P = 0.0002 and P = 0.0003, respectively). The results suggest that lycopene supplementation may decrease the growth of prostate cancer. However, no firm conclusions can be drawn at this time because of the small **sample size**
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L46 ANSWER 16 OF 26 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
DUPLICATE

ACCESSION NUMBER: 2001:32998807 BIOTECHNO
TITLE: **Biomarker** correlations of urinary 2,4-D levels in foresters: Genomic instability and endocrine disruption
AUTHOR: Garry V.F.; Tarone R.E.; Kirsch I.R.; Abdallah J.M.; Lombardi D.P.; Long L.K.; Burroughs B.L.; Barr D.B.; Kesner J.S.
CORPORATE SOURCE: V.F. Garry, Environ. Med./Pathology Laboratory, University of Minnesota, 421 29th Avenue SE, Minneapolis, MN 55414-3290, United States. E-mail: garry001@maroon.tc.umn.edu
SOURCE: Environmental Health Perspectives, (**2001**), 109/5 (495-500), 28 reference(s) CODEN: EVHPAZ ISSN: 0091-6765
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 2001:32998807 BIOTECHNO
AB Forest pesticide applicators constitute a unique pesticide use group. Aerial, mechanical-ground, and focal weed control by application of herbicides, in particular chlorophenoxy herbicides, yield diverse exposure scenarios. In the present work, we analyzed aberrations in G-banded chromosomes, reproductive hormone levels, and polymerase chain reaction-based V(D)J rearrangement frequencies in applicators whose exposures were mostly limited to chlorophenoxy herbicides. Data from appliers where chlorophenoxy use was less frequent were also examined. The **biomarker** outcome data were compared to urinary levels of 2,4-dichlorophenoxyacetic acid (2,4-D) obtained at the time of maximum 2,4-D use. Further comparisons of outcome data were made to the total volume of herbicides applied during the entire pesticide-use season. Twenty-four applicators and 15 minimally exposed foresters (control) subjects were studied. Categorized by applicator method, men who used a hand-held, backpack sprayer in their applications showed the highest average level (453.6 ppb) of 2,4-D in urine. Serum luteinizing hormone (LH) values were correlated with urinary 2,4-D levels, but follicle-stimulating hormone and free and total testosterone were not. At the height of the application season; 6/7 backpack sprayers, 3/4 applicators who used multinozzle mechanical (boom) sprayers, 4/8 aerial applicators, and 2/5 skidder-radiarc (closed cab) appliers had two or more V(D)J region rearrangements per microgram of DNA. Only 5 of 15 minimally exposed (control) foresters had two or more rearrangements, and 3 of these 5 subjects demonstrated detectable levels of 2,4-D in the urine. Only 8/24 DNA samples obtained from the exposed group 10 months or more after their last chlorophenoxy use had two rearrangements per microgram of DNA, suggesting that the exposure-related effects observed were reversible and temporary. Although urinary 2,4-D levels were not correlated with chromosome aberration frequency, chromosome aberration frequencies were correlated with the total volume of herbicides applied, including products other than 2,4-D. In summary, herbicide applicators with high urinary levels of 2,4-D (backpack and boom spray applications) exhibited elevated LH levels. They also exhibited altered genomic stability as measured by V(D)J rearrangement frequency, which appears reversible months after peak exposure. Though highly detailed, the limited **sample size** warrants cautious interpretation of the data.

L46 ANSWER 17 OF 26 BIOTECHNO
DUPLICATE
ACCESSION NUMBER: 2001:32592065 BIOTECHNO
TITLE: In vitro BPDE-induced DNA adducts in peripheral lymphocytes as a risk factor for squamous cell carcinoma of the head and neck
AUTHOR: Li D.; Firozi P.F.; Chang P.; Wang L.-E.; Xiong P.;

Sturgis E.M.; Eicher S.A.; Spitz M.R.; Hong W.-K.; Wei Q.

CORPORATE SOURCE: D. Li, Dept. Gastrointestinal Med. Oncology, Box 426, Univ. Texas M. D. Anderson Can. Ctr., 1515 Holcombe Boulevard, Houston, TX 77030, United States. E-mail: dli@mdanderson.org

SOURCE: International Journal of Cancer, **(01 AUG 2001)**, 93/3 (436-440), 27 reference(s) CODEN: IJCNAW ISSN: 0020-7136

DOCUMENT TYPE: Journal; Article

COUNTRY: United States

LANGUAGE: English

SUMMARY LANGUAGE: English

AN 2001:32592065 BIOTECHNO

AB The level of DNA adducts under the same conditions of carcinogen exposure and cell proliferation reflects an integrated measure of carcinogen metabolism and DNA repair. Therefore, such DNA adduct levels have the potential to be a **biomarker** for susceptibility to chemical carcinogenesis. In a pilot study of 91 patients with squamous cell carcinomas of the head and neck and 115 controls who were frequency matched by age, sex, ethnicity, and smoking status, we applied a newly developed in vitro assay of benzo[a]pyrene diol epoxide (BPDE)-induced DNA adducts in short-term peripheral lymphocytes cultures. Levels of BPDE-DNA adducts were found to be significantly higher in cases than in controls (mean ± SD, 76.8 ± 77.4/10.sup.7 and 47.1 ± 48.0/10.sup.7 nucleotides, respectively; $p < 0.001$). Using the median level of control values (35/10.sup.7) as the cut-off point, about 66% of cases were distributed above this level. Logistic regression analysis revealed that the level of BPDE-induced DNA adducts was an independent risk factor (odds ratio = 2.22; 95% confidence interval = 1.22-4.04) after adjustment for age, sex and smoking status. Further stratified analyses showed that levels of the induced adducts between cases and controls were significantly higher in both age groups, that is, younger or older than 60, as well as in both men and women. Smoking had a positive effect on the induced adducts. The highest level of induced adducts was seen in current smokers, then former smokers and non-smokers. There was a statistically significant dose-response relationship between the quartile levels of BPDE-induced DNA adducts and the risk of head and neck cancer (trend test, $p = 0.003$). Despite the relatively small **sample size**, the association of BPDE-induced DNA adducts and cancer risk suggests that this assay has the potential to complement with other **biomarkers** in identifying individuals at increased risk of developing tobacco-related cancers. .COPYRGT. 2001 Wiley-Liss, Inc.

L46 ANSWER 18 OF 26 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN DUPLICATE

ACCESSION NUMBER: 2001:32707745 BIOTECHNO

TITLE: Effect of TCDD exposure on CYP1A1 and CYP1B1 expression in explant cultures of human endometrium

AUTHOR: Bofinger D.P.; Feng L.; Chi L.-H.; Love J.; Stephen F.D.; Sutter T.R.; Osteen K.G.; Costich T.G.; Batt R.E.; Koury S.T.; Olson J.R.

CORPORATE SOURCE: D.P. Bofinger, Department of Biotechnical, Clinical Laboratory Science, State University of New York, 3435 Main Street, Buffalo, NY 14214, United States. E-mail: dbofinge@acsu.buffalo.edu

SOURCE: Toxicological Sciences, **(2001)**, 62/2 (299-314), 85 reference(s) CODEN: TOSCF2 ISSN: 1096-6080

DOCUMENT TYPE: Journal; Article

COUNTRY: United States

LANGUAGE: English

SUMMARY LANGUAGE: English

AN 2001:32707745 BIOTECHNO
AB Endometriosis is a debilitating disease estimated to affect 10% of reproductive-age women and characterized by the growth of endometrial tissue outside of the uterus. The present study characterizes a human endometrial explant culture model for studying the direct effects of TCDD exposure by assessing the expression of CYP1A1 and CYP1B1 mRNA (Northern blotting), protein (Western blotting), and activity (7-ethoxyresorufin-O-deethylase; EROD) in explants cultured with and without TCDD. Explants were obtained at laparoscopy or laparotomy from women undergoing surgery for tubal ligation, endometriosis, or pelvic pain unrelated to endometriosis. The explants were cultured with 10 nM estradiol (E.sub.2) or 1 nM E.sub.2 plus 500 nM progesterone (P.sub.4) with or without TCDD (first 24 h). The expression of CYP1A1 and CYP1B1 mRNA was greatest with 10 nM TCDD and increased up to 72 h after initial exposure. EROD activity increased up to 120 h. Explants from a secretory phase biopsy became reorganized in culture and formed a new epithelial membrane, while maintaining basic endometrial morphology and viability for up to 120 h. At 24 h, TCDD significantly increased CYP1A1 and CYP1B1 mRNA, and at 72 h, TCDD significantly increased EROD activity and CYP1B1 protein compared to explants cultured without TCDD for similar times. CYP1B1 protein also exhibited substantial constitutive expression that was similar in uncultured biopsies, where CYP1B1 protein was immunolocalized in the cytoplasm of epithelial glands, with only occasional patches of protein in the surface epithelial membrane. In explants cultured with and without TCDD exposure, CYP1B1 protein was localized in the cytoplasm of the new surface epithelial membrane and glands closest to the surface. CYP1A1 protein was not detected in uncultured biopsies or explants. Both younger age (age 30 and under) and proliferative phase were associated with higher TCDD-induced EROD activity in specimens treated with E.sub.2:P.sub.4. No significant endometriosis-related differences were observed for any of the **biomarkers**, but the detection of disease-specific change was limited by small **sample size** and variability in tissue-cycle phase. The human endometrial explant culture model will be useful for future studies of the effects of dioxin-like compounds on human endometrium in relationship to cycle phase and hormonal exposure.

L46 ANSWER 19 OF 26 PASCAL COPYRIGHT 2004 INIST-CNRS. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2001-0236308 PASCAL
COPYRIGHT NOTICE: Copyright .COPYRGT. 2001 INIST-CNRS. All rights reserved.
TITLE (IN ENGLISH): Prostate cancer chemoprevention : Strategies for designing efficient clinical trials
AUTHOR: LIEBERMAN Ronald
CORPORATE SOURCE: National Cancer Institute, Rockville, Maryland, United States
SOURCE: Urology : (Ridgewood, NJ), **(2001)**, 57(4A), 224-229, 23 refs.
ISSN: 0090-4295 CODEN: URGYAZ
DOCUMENT TYPE: Journal
BIBLIOGRAPHIC LEVEL: Analytic
COUNTRY: United States
LANGUAGE: English
AVAILABILITY: INIST-15471, 354000098139820440
AN 2001-0236308 PASCAL
CP Copyright .COPYRGT. 2001 INIST-CNRS. All rights reserved.
AB A chemoprevention (CP) strategy has evolved for conducting efficient clinical trials for prostate cancer (PCa) prevention. It integrates five key components, including agents, **biomarkers**, cohorts, designs, and endpoints. The rationale for the CP strategy relates to the natural history of prostate cancer. There is a wide array of natural and synthetic agents that hold promise for inhibiting, reversing, or modulating the transition from normal to precancer and from precancer to

cancer. These agent classes include antiandrogens, antiestrogens, phytoestrogens, antioxidants, anti-inflammatory (proapoptotic) agents, antiproliferation/antidifferentiation agents, signal transduction modulators of receptor tyrosine kinase and ras farnesylation, antiangiogenesis agents, insulinlike growth factor (IGF)-1, peroxisome proliferator-activator receptor modulators (-γ and -δ), and gene-based interventions. **Biomarkers** and endpoints are guided by the level of evidence required (eg, phase 1, 2, 3). Two candidate surrogate endpoints (SE) based on histology are high-grade prostatic intraepithelial neoplasia (HGPIN) and computer-assisted image analysis of dysplastic lesions. Phase 1 trials use standard endpoints of safety, pharmacokinetics and limited pharmacodynamics. Phase 2 trials use endpoints of modulation of **biomarkers** and correlation with histology. Phase 3 trials use endpoints of clinical benefit, such as cancer incidence reduction and quality of life. Validation of a **biomarker** as a SE involves correlation of the **biomarker** with clinical benefit. Cohorts (target populations) for phase 2/3 trials include the general population of men over age 50 with a normal prostate-specific antigen (PSA), subjects with a strong family history of PCa, subjects with elevated PSA/negative biopsy, and subjects with HGPIN/negative biopsy. These at-risk populations reflect key individual risk factors (age, race, serum PSA [free/total]; serum IGF- 1/IGF binding protein (IGFBP)-3; 1, 25(OH).sub.2D3; family history of PCa; carriers of PCa susceptibility genes [ELAC2, CYP3A4, SRD5A2, etc.]; and histology such as atypia and HGPIN) that could be combined into a multivariate risk model for PCa. The probability of cancer risk (recurrence) is a key factor that impacts on the clinical trial design (power, **sample size**, and primary endpoint). Multivariate predictive mathematical models for biochemical recurrence after radical prostatectomy by decreasing **sample size** and time to clinical outcomes maximize trial efficiency and identify the patients most likely to benefit from secondary prevention. The two large primary prevention trials, Prostate Cancer Prevention Trial/Seleninium and Vitamin E Chemoprevention Trial (PCPT/ SELECT), in low- and average-risk subjects have **sample sizes** of 18,000 to 32,000, with a treatment duration of 7 years to detect a 25% reduction in biopsy-proven PCa. Subjects with HGPIN have the highest known cancer risk (approximately 50% at 3 years), and thus require a small **sample size** (n = 450) to detect a 33% reduction in cancer incidence. A schema involving three sequential trials for agent registration is described. In summary, a CP strategy that incorporates well-defined agents, clinical and validated SE, and high-risk cohorts defined by genetic and acquired risk factors in a series of well-designed randomized controlled trials provides an efficient pathway for evaluating and approving new agents for PCa prevention.

L46 ANSWER 20 OF 26 HEALSAFE COPYRIGHT 2004 CSA on STN DUPLICATE 8
ACCESSION NUMBER: 2001:3051 HEALSAFE
TITLE: Usefulness of Genetic Susceptibility and **Biomarkers** for Evaluation of Environmental Health Risk
AUTHOR: Au, W.W.; Oh, H.Y.; Grady, J.; Salama, S.A.; Heo, M.Y.
CORPORATE SOURCE: The University of Texas Medical Branch, Department of Preventive Medicine and Community Health, Galveston, TX 77555-1110, USA; E-mail: william.au@utmb.edu
SOURCE: Environmental and Molecular Mutagenesis [Environ. Mol. Mutag.], (**20010000**) vol. 37, no. 3, pp. 215-225. ISSN: 0893-6692.
DOCUMENT TYPE: Journal
FILE SEGMENT: H
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Recent attention is focused on understanding the genetic basis for individual susceptibility to the development of chronic disease. An emphasis is concentrated on establishing an association between

inheritance of polymorphic chemical metabolizing genes and development of environmental cancer (e.g., lung cancer among cigarette smokers). The early reports of such associations have been very encouraging. However, some reported positive associations were not substantiated in subsequent studies using larger **sample sizes** and different ethnic populations. In this review, some confounding factors that contribute to the discrepancies are presented (e.g., ethnic-dependent distribution of variant gene alleles, differential expression of metabolizing genes, and inadequate study design). It is possible that the precision of the association can be improved if the mentioned investigations are complemented with concurrent studies of biological activities/effects. The usefulness of integrating metabolic susceptibility with **biomarker** measurement for understanding the development of lung cancers is presented. The importance of using adequate **sample size** and experimental design is emphasized. Development of a reliable approach for prediction of environmental disease not only will provide fundamental information regarding the genetic basis of human disease but will be useful for reducing disease burden in the population and for advancing patient care.

L46 ANSWER 21 OF 26 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
DUPLICATE

ACCESSION NUMBER: 2001:34001705 BIOTECHNO
TITLE: Effects of contaminants on genetic patterns in aquatic organisms: A review
AUTHOR: Belfiore N.M.; Anderson S.L.
CORPORATE SOURCE: N.M. Belfiore, Department of Animal Science, University of California, Davis, CA 95616, United States.
E-mail: nmbelfiore@fnr.purdue.edu
SOURCE: Mutation Research - Reviews in Mutation Research, (**2001**), 489/2-3 (97-122), 144 reference(s)
CODEN: MRRRFK ISSN: 1383-5742
PUBLISHER ITEM IDENT.: S1383574201000655
DOCUMENT TYPE: Journal; Article
COUNTRY: Netherlands
LANGUAGE: English
SUMMARY LANGUAGE: English

AN 2001:34001705 BIOTECHNO
AB There is increasing awareness of the need to evaluate the effects of contaminants at the population level. Genetic techniques offer a powerful approach to assess contaminant-induced changes in populations. Yet studies to date are relatively few and not always carefully designed to maximize the utility inherent in this approach. We present a summary of contemporary genetic assessment methods and a review of published studies of genetic effects in field-exposed aquatic organisms. We discuss evaluations of genetic patterns that use genetic adaptation, allozyme variation, and molecular genetic (DNA) variation. Direct tests of genetic adaptation are very effective in establishing a concrete, and potentially deleterious population-level effect of contaminant exposure, but they are difficult to accomplish with most field-exposed organisms. Allozyme surveys are relatively simple and common, and may provide data that are suggestive of contaminant effects. However, these are rarely conclusive, primarily because few allozyme loci are variable and these few loci represent extremely small portions of the genome. Molecular genetic techniques have the potential to be very effective. But, there is a tendency to emphasize the power of the techniques, rather than the underlying causes of the molecular genetic patterns observed. The strength of the conclusions of each study varies widely, partially derived from variation in the strength of the techniques. We caution that all these approaches are greatly improved by careful experimental design that includes adequate numbers of reference and contaminated sites and **sample size**. In addition, careful exposure assessment is required, including site and tissue chemistry, **biomarker**

responses, and measures of potentially deleterious effects, such as DNA damage, or reduced reproductive output or survival. .COPYRGT. 2001 Elsevier Science B.V. All rights reserved.

L46 ANSWER 22 OF 26 PASCAL COPYRIGHT 2004 INIST-CNRS. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2001-0387416 PASCAL
COPYRIGHT NOTICE: Copyright .COPYRGT. 2001 INIST-CNRS. All rights reserved.
TITLE (IN ENGLISH): Serum thiocyanate concentration as an indicator of smoking in relation to deaths from cancer
AUTHOR: WANG Hongbing; SEKINE Michikazu; YOKOKAWA Hiroshi; HAMANISHI Shimako; SAYAMA Michio; NARUSE Yuchi; NAKAGAWA Hideaki; KAGAMIMORI Sadanobu
CORPORATE SOURCE: Department of Welfare Promotion and Epidemiology, Toyama Medical and Pharmaceutical University, Toyama, Japan; Faculty of Engineering, Toyama University, Toyama, Japan; Department of Community and Geriatric Nursing, Toyama Medical and Pharmaceutical University, Toyama, Japan; Department of Public Health, Kanazawa Medical University, Ishikawa, Japan
SOURCE: Environmental health and preventive medicine, **(2001)**, 6(2), 88-91, 19 refs.
ISSN: 1342-078X
DOCUMENT TYPE: Journal
BIBLIOGRAPHIC LEVEL: Analytic
COUNTRY: Japan
LANGUAGE: English
AVAILABILITY: INIST-26502, 354000097165810040

AN 2001-0387416 PASCAL
CP Copyright .COPYRGT. 2001 INIST-CNRS. All rights reserved.
AB All residents aged 40 years or more in Oyabe City, Toyama Prefecture, Japan were involved in an annual medical check-up between 1987 and 1988. The cohort was followed and death certificates from cancers were confirmed prospectively. During follow-up to December 31st, 1994, 100 deaths (28 gastric, 17 lung and 55 other cancers) from cancers occurred, and these subjects were included in this study as the case group. Subjects in the control group, matched for gender and age with the cases, were selected randomly from participants whose serum samples had been stocked during annual medical check-up. The concentration of serum thiocyanate in all (79.8 μmol/l), gastric (86.7 μmol/l) and lung (90.0 μmol/l) cancer patients were significantly higher than that of relevant controls (64.3 μmol/l, 59.0 μmol/l and 61.0 μmol/l, respectively; and $p<0.001$, $p<0.001$ and $p<0.05$, respectively). After adjusting for BMI, blood pressure and total serum cholesterol, the results of multiple logistic regression analysis showed that the risk of all cancers (OR=3.40, 95% confidence interval (95% CI): 1.67-6.96, $p<0.01$), gastric cancer (OR=7.98, 95% CI: 1.91-33.34, $p<0.05$) and lung cancer (OR=8.83, 95% CI: 1.19-65.65, $p<0.05$) were elevated significantly with logarithm transformed values of serum thiocyanate increased. The present findings suggested that in epidemiological studies confirmation of smoking status with **biomarkers** such as serum thiocyanate may be important, although considering the small **sample size**, a relatively weaker risk to interested factors rather than the strong relationship between smoking and cancer was noted.

L46 ANSWER 23 OF 26 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN

ACCESSION NUMBER: 2001:33031896 BIOTECHNO
TITLE: An application of the challenge assay in boat builders exposed to low levels of styrene - A feasibility study of a possible **biomarker** for acquired susceptibility
AUTHOR: Oberheitmann B.; Frentzel-Beyme R.; Hoffmann W.
CORPORATE SOURCE: Dr. B. Oberheitmann, Ctr. Environ. Res./Environ.

Technol., Division of Epidemiology, University of Bremen, D-28334 Bremen, Germany.
E-mail: boris@oberheitmann.de

SOURCE: International Journal of Hygiene and Environmental Health, (2001), 204/1 (23-29), 39 reference(s)
CODEN: IJEHFT ISSN: 1438-4639
DOCUMENT TYPE: Journal; Conference Article
COUNTRY: Germany, Federal Republic of
LANGUAGE: English
SUMMARY LANGUAGE: English

AN 2001:33031896 BIOTECHNO

AB Sensitivity to carcinogens and susceptibility for malignant diseases may be related to genetic predisposition, e.g. polymorphisms in toxicant-metabolizing enzymes or DNA repair deficiencies. The latter may also be acquired by exposure to substances that interfere with DNA repair processes. Application of the challenge assay to an exposed population may allow scientists to study the interference of DNA repair as an acquired susceptibility phenomenon. The assay was therefore used in a feasibility study to evaluate its application. A group of 14 workers exposed to low levels of styrene (mean < 100 mg/m.sup.3 styrene in air; 35 µg/l styrene in blood) and a reference of seven controls were investigated for structural chromosomal aberrations using FISH. The rate of exchange-type aberrations per 100 metaphases was 0.14 (95% CI, 0.05-0.31) in controls and 0.22 (95% CI, 0.13-0.36) in exposed workers. The difference is not statistically significant. Interaction with DNA repair was measured in the 14 workers and 2 historical controls using the challenge assay. Exchange-type aberrations per 100 metaphases after X-ray challenge of 1.66 Gy were 13.26 (10.53-16.50) and 16.19 (15.00-17.40) for the controls and exposed, respectively. The difference is statistically significant (p<0.038). Among the exposed group, the challenge response was also significantly correlated with the cumulative lifetime exposure to styrene (R.sup.2 = 0.3996; p<0.015) but not with the current exposure as measured in blood (R.sup.2=0.0226; p=0.700). The challenge responses in the short-term and long-term exposed subgroups were 15.55 (14.23-16.96) and 17.90 (15.64-20.39), respectively, based on **sample sizes** of 5 and 9, respectively. The difference was not significant. Hence, data from our study are consistent with the hypothesis that long-term exposure to styrene can interfere with DNA repair activities. The lack of statistically significant differences in some of the data may be due to the small sample size and a possible confounding by age in our investigation. Additional data from our ongoing study should clarify this uncertainty.

L46 ANSWER 24 OF 26 PASCAL on STN

ACCESSION NUMBER: 2001-0128819 PASCAL

TITLE (IN ENGLISH): Analysis and design issues for studies using censored **biomarker** measurements with an example of viral load measurements in HIV clinical trials
Current Perspectives and Future Directions in Medical Statistics

AUTHOR: HUGHES Michael D.
POCOCK Stuart (ed.); ELBOURNE Diana (ed.)
CORPORATE SOURCE: Department of Biostatistics, Harvard School of Public Health, 655 Huntington Avenue, Boston, Massachusetts 02115, United States
Medical Statistics Unit, London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT, United Kingdom
Royal Statistical Society. Medical Section, London, United Kingdom (patr.); London School of Hygiene and

Tropical Medicine, London, United Kingdom (patr.)
SOURCE: Statistics in medicine, **(2000)**, 19(23), 3171-3191, 20 refs.
Conference: Current Perspectives and Future Directions in Medical Statistics. Conference, London (United Kingdom), 15 Apr 1999
ISSN: 0277-6715
DOCUMENT TYPE: Journal; Conference
BIBLIOGRAPHIC LEVEL: Analytic
COUNTRY: United Kingdom
LANGUAGE: English
AVAILABILITY: INIST-19624, 354000093354650030
AN 2001-0128819 PASCAL

AB For many **biomarkers**, the range (L,R) over which they can be quantified is restricted by technical limitations, leading to some measurements that are left or right censored. However, despite the widespread availability of statistical methods for the analysis of censored data, many studies use an imputed value for censored measurements (for example, replacing a value <L by L, or by L/2). Commonly, an analysis that ignores such imputation is then used. In clinical trials, this leads to bias and a loss of power in evaluating treatment effects. In this paper, a review of appropriate statistical methods for parametric and non-parametric analysis of such measurements is presented. This includes methods for situations in which baseline measurements are available. New results concerning design issues such as **sample size** determination are also presented. The paper is illustrated using two examples of studies that included censored measurements of viral load in HIV-infected subjects.

L46 ANSWER 25 OF 26 PASCAL on STN
ACCESSION NUMBER: 2000-0537908 PASCAL

TITLE (IN ENGLISH): Novel translational model for breast cancer chemoprevention study : Accrual to a presurgical intervention with tamoxifen and N-[4-hydroxyphenyl] retinamide
AUTHOR: SINGLETARY Eva; LIEBERMAN Ron; ATKINSON Nealy; SNEIGE Nour; SAHIN Ayse; TOLLEY Susanne; COLCHIN Mary; BEVERS Therese; STELLING Carol; FORNAGE Bruno; FRITSCHE Herbert; HITTELMAN Walter; KELLOFF Gary; LIPPMAN Scott M.
CORPORATE SOURCE: The University of Texas M. D. Anderson Cancer Center, Houston, Texas 77030, United States; National Cancer Institute, Chemoprevention Branch, Bethesda, Maryland 20852, United States
SOURCE: Cancer epidemiology, biomarkers & prevention, **(2000)**, 9(10), 1087-1090, 18 refs.
ISSN: 1055-9965
DOCUMENT TYPE: Journal
BIBLIOGRAPHIC LEVEL: Analytic
COUNTRY: United States
LANGUAGE: English
AVAILABILITY: INIST-26637, 354000092661650120
AN 2000-0537908 PASCAL

AB Surrogate end point **biomarkers** for risk assessment and efficacy of potential chemopreventive agents are needed to improve the efficiency and reduce the cost of chemoprevention trials. It is imperative to develop the best clinical breast model for translational surrogate end point **biomarker** studies, especially with respect to accrual feasibility. We have initiated a prospective study to develop

biomarkers for tamoxifen and N-[4-hydroxyphenyl] retinamide by administering either a placebo or both drugs for 2-4 weeks to women with ductal carcinoma in situ or early invasive cancers in the interval between the initial diagnostic core biopsy and definitive surgery. The principle end point is pretreatment versus posttreatment tumor levels of Ki-67; a number of other exploratory markers will also be examined. The planned target **sample size** is 100 patients. Between February 1997 and February 2000, 4514 women who had either an abnormal mammogram or a diagnosed breast cancer were screened for the study. Of these 4514 screened patients, 52 (1%) were registered on the study. Major factors of nonparticipation in the remaining 4462 women were as follows: (a) no evidence of malignancy (2081 patients; 46%); (b) ineligible per protocol criteria (575 patients; 13%); (c) preoperative chemotherapy/tamoxifen (520 patients; 11%); (d) surgery scheduling conflict (360 patients; 8%); (e) outside needle biopsy (221 patients; 5%); (f) no residual disease after excisional biopsy (345 patients; 8%); and (g) second opinion only (123 patients; 3%). Other nonparticipation factors included fine needle aspiration only, refusal, tumor size > 2 cm, and estrogen replacement therapy (35 patients each; 2% each). The protocol was amended in midstudy to allow outside needle biopsy, tumor > 2 cm, and estrogen replacement therapy. Accrual to **biomarker** (nontherapeutic) protocols with delay in definitive cancer surgery is challenging but feasible. Although some accrual problems remain, we have nonetheless succeeded in recruiting 50% of our target **sample size** in a 3-year period.

L46 ANSWER 26 OF 26 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
DUPLICATE

ACCESSION NUMBER: 2000:30451657 BIOTECHNO
TITLE: A polymorphism in the CYP17 genie is associated with prostate cancer risk
AUTHOR: Gsur A.; Bernhofer G.; Hinteregger S.; Haidinger G.; Schatzl G.; Madersbacher S.; Marberger M.; Vutuc C.; Micksche M.
CORPORATE SOURCE: A. Gsur, Dept. of Applied and Exp. Oncology, Institute of Cancer Research, Borschkegasse 8a, 1090 Vienna, Austria.
E-mail: andrea.gsur@univie.ac.at
SOURCE: International Journal of Cancer, **(01 AUG 2000)** , 87/3 (434-437), 22 reference(s)
CODEN: IJCNAW ISSN: 0020-7136
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English

AN 2000:30451657 BIOTECHNO

AB CYP17 encodes the enzyme cytochrome P-450c17α, which mediates both 17α-hydroxylase and 17,20-Lyase in the steroid biosynthesis pathway. A polymorphism in the 5' promoter region of the CYP17 gene has been described. Steroid hormones, especially androgens, are believed to play a key role in the etiology of prostate cancer. Therefore, polymorphisms in genes involved in the androgen metabolism may affect the risk of prostate cancer. We conducted a case-control study of 63 patients with untreated histologically proven prostate cancer and 126 age-matched control men with benign prostatic hyperplasia (BPH) to determine whether a polymorphism in the CYP17 gene is associated with prostate cancer risk. This polymorphism was investigated by PCR/RFLP using DNA from lymphocytes. The transition (T→C) in the risk allele (A2) creates a new recognition site for the restriction enzyme MspA1, which permits designation of the wildtype (A1) and the risk allele (A2). The prevalence of the A2/A2 genotype was significantly higher (P = 0.03) in the cancer group (23.8%) than in the BPH control group (9.5%). We found an increased risk in men carrying 2 A2 alleles (OR = 2.80, 95% CI = 1.02-77.76). For carrier with at least I A2 allele, the OR was 0.90 (95% CI = 0.43-1.89).

After stratification by median age (66 years) at time of diagnosis, a marked increased risk was found in carriers of the A2/A2 genotype older than 66 years (OR = 8.93, 95% CI = 1.78-49.19, P = 0.01). Although the **sample size** is rather small and the controls are BPH patients, our results suggest that the CYP17A2/A2 genotype may be a **biomarker** for prostate cancer risk, especially for older men. (C) 2000 Wiley-Liss, Inc.

```
=> (sample size)(5A)(need or require)
L47          17 FILE AGRICOLA
L48          38 FILE BIOTECHNO
L49           0 FILE CONFSCI
L50           8 FILE HEALSAFE
L51           0 FILE IMSDRUGCONF
L52          83 FILE LIFESCI
L53           0 FILE MEDICONF
L54         181 FILE PASCAL

TOTAL FOR ALL FILES
L55         327 (SAMPLE SIZE)(5A)(NEED OR REQUIRE)

=> l55 and biomarker
L56           0 FILE AGRICOLA
L57           0 FILE BIOTECHNO
L58           0 FILE CONFSCI
L59           0 FILE HEALSAFE
L60           0 FILE IMSDRUGCONF
L61           0 FILE LIFESCI
L62           0 FILE MEDICONF
L63           1 FILE PASCAL

TOTAL FOR ALL FILES
L64           1 L55 AND BIOMARKER

=> d l64 ibib abs total

L64   ANSWER 1 OF 1  PASCAL  COPYRIGHT 2004 INIST-CNRS. ALL RIGHTS RESERVED. on
      STN
ACCESSION NUMBER:         2001-0236308   PASCAL
COPYRIGHT NOTICE:         Copyright .COPYRGT. 2001 INIST-CNRS. All rights
                          reserved.
TITLE (IN ENGLISH):       Prostate cancer chemoprevention : Strategies for
                          designing efficient clinical trials
AUTHOR:                   LIEBERMAN Ronald
CORPORATE SOURCE:         National Cancer Institute, Rockville, Maryland, United
                          States
SOURCE:                   Urology : (Ridgewood, NJ), (2001), 57(4A), 224-229, 23
                          refs.
                          ISSN: 0090-4295  CODEN: URGYAZ
DOCUMENT TYPE:            Journal
BIBLIOGRAPHIC LEVEL:      Analytic
COUNTRY:                  United States
LANGUAGE:                 English
AVAILABILITY:             INIST-15471, 354000098139820440
AN    2001-0236308   PASCAL
CP    Copyright .COPYRGT. 2001 INIST-CNRS. All rights reserved.
AB    A chemoprevention (CP) strategy has evolved for conducting efficient
      clinical trials for prostate cancer (PCa) prevention. It integrates five
      key components, including agents, biomarkers, cohorts, designs,
      and endpoints. The rationale for the CP strategy relates to the natural
      history of prostate cancer. There is a wide array of natural and
      synthetic agents that hold promise for inhibiting, reversing, or
      modulating the transition from normal to precancer and from precancer to
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cancer. These agent classes include antiandrogens, antiestrogens, phytoestrogens, antioxidants, anti-inflammatory (proapoptotic) agents, antiproliferation/antidifferentiation agents, signal transduction modulators of receptor tyrosine kinase and ras farnesylation, antiangiogenesis agents, insulinlike growth factor (IGF)-1, peroxisome proliferator-activator receptor modulators (-y and -δ), and gene-based interventions. **Biomarkers** and endpoints are guided by the level of evidence required (eg, phase 1, 2, 3). Two candidate surrogate endpoints (SE) based on histology are high-grade prostatic intraepithelial neoplasia (HGPIN) and computer-assisted image analysis of dysplastic lesions. Phase 1 trials use standard endpoints of safety, pharmacokinetics and limited pharmacodynamics. Phase 2 trials use endpoints of modulation of **biomarkers** and correlation with histology. Phase 3 trials use endpoints of clinical benefit, such as cancer incidence reduction and quality of life. Validation of a **biomarker** as a SE involves correlation of the **biomarker** with clinical benefit. Cohorts (target populations) for phase 2/3 trials include the general population of men over age 50 with a normal prostate-specific antigen (PSA), subjects with a strong family history of PCa, subjects with elevated PSA/negative biopsy, and subjects with HGPIN/negative biopsy. These at-risk populations reflect key individual risk factors (age, race, serum PSA [free/total]; serum IGF- 1/IGF binding protein (IGFBP)-3; 1, 25(OH).sub.2D3; family history of PCa; carriers of PCa susceptibility genes [ELAC2, CYP3A4, SRD5A2, etc.]; and histology such as atypia and HGPIN) that could be combined into a multivariate risk model for PCa. The probability of cancer risk (recurrence) is a key factor that impacts on the clinical trial design (power, sample size, and primary endpoint). Multivariate predictive mathematical models for biochemical recurrence after radical prostatectomy by decreasing sample size and time to clinical outcomes maximize trial efficiency and identify the patients most likely to benefit from secondary prevention. The two large primary prevention trials, Prostate Cancer Prevention Trial/Seleninium and Vitamin E Chemoprevention Trial (PCPT/ SELECT), in low- and average-risk subjects have sample sizes of 18,000 to 32,000, with a treatment duration of 7 years to detect a 25% reduction in biopsy-proven PCa. Subjects with HGPIN have the highest known cancer risk (approximately 50% at 3 years), and thus **require** a small **sample size** (n = 450) to detect a 33% reduction in cancer incidence. A schema involving three sequential trials for agent registration is described. In summary, a CP strategy that incorporates well-defined agents, clinical and validated SE, and high-risk cohorts defined by genetic and acquired risk factors in a series of well-designed randomized controlled trials provides an efficient pathway for evaluating and approving new agents for PCa prevention.

```
=> (sample size)(5A)(required or needed)
L65          91 FILE AGRICOLA
L66         111 FILE BIOTECHNO
L67           6 FILE CONFSCI
L68          11 FILE HEALSAFE
L69           0 FILE IMSDRUGCONF
L70         206 FILE LIFESCI
L71           0 FILE MEDICONF
L72         567 FILE PASCAL

TOTAL FOR ALL FILES
L73         992 (SAMPLE SIZE)(5A)(REQUIRED OR NEEDED)

=> l73 and biomarker
L74           0 FILE AGRICOLA
L75           0 FILE BIOTECHNO
L76           0 FILE CONFSCI
L77           1 FILE HEALSAFE
```

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L78           0 FILE IMSDRUGCONF
L79           2 FILE LIFESCI
L80           0 FILE MEDICONF
L81           1 FILE PASCAL

TOTAL FOR ALL FILES
L82           4 L73 AND BIOMARKER

=> dup rem
ENTER L# LIST OR (END):l82
DUPLICATE IS NOT AVAILABLE IN 'IMSDRUGCONF, MEDICONF'.
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
PROCESSING COMPLETED FOR L82
L83            2 DUP REM L82 (2 DUPLICATES REMOVED)

=> d l83 ibib abs total

L83  ANSWER 1 OF 2  HEALSAFE  COPYRIGHT 2004 CSA on STN DUPLICATE 1
ACCESSION NUMBER:   1999:2743  HEALSAFE
TITLE:              Methodological issues in biomonitoring of low level
                    exposure to benzene
AUTHOR:             Lagorio, S.; Crebelli, R.; Ricciarello, R.; Conti, L.;
                    Iavarone, I.; Zona, A.; Ghittori, S.; Carere, A.
CORPORATE SOURCE:   Istituto Superiore di Sanita, Laboratorio Igiene
                    Ambientale, Viale Regina Elena, 299, 00161 Rome, Italy;
                    E-mail: lagorio@pop3.iss.it
SOURCE:             Occupational Medicine [Occup. Med.], (19981100) vol. 48,
                    no. 8, pp. 497-504.
                    ISSN: 0962-7480.
DOCUMENT TYPE:      Journal
FILE SEGMENT:       H
LANGUAGE:           English
SUMMARY LANGUAGE:   English
AB   Data from a pilot study on unmetabolized benzene and trans,trans muconic
     acid (t,t-MA) excretion in filling station attendants and unexposed
     controls were used to afford methodological issues in the biomonitoring of
     low benzene exposures (around 0.1 ppm). Urinary concentrations of benzene
     and t,t-MA were measured by dynamic head-space capillary GC/FID and HPLC,
     respectively. The accuracy of the HPLC determination of t,t-MA was
     assessed in terms of inter- and intra-method reliability. The adequacy of
     urinary t,t-MA and benzene as biological markers of low benzene exposure
     was evaluated by analysing the relationship between personal exposure to
     benzene and biomarker excretion. Filling station attendants
     excreted significantly higher amounts of benzene, but not of t,t-MA, than
     controls. Adjusting for occupational benzene exposure, smokers excreted
     significantly higher amounts of t,t-MA, but not of unmetabolized benzene,
     than nonsmokers. A comparative analysis of the present and previously
     published biomonitoring surveys showed a good inter-study agreement
     regarding the amount of t,t-MA and unmetabolized benzene excreted (about
     0.1-0.2 mg/l and 1-2 mu g/l, respectively) per unit of exposure (0.1 ppm).
     For each biomarker, based on the distribution of parameters
     observed in the pilot study, we calculated the minimum sample
     size required to estimate the population mean with given
     confidence and precision.

L83  ANSWER 2 OF 2  LIFESCI    COPYRIGHT 2004 CSA on STN
ACCESSION NUMBER:   95:106966  LIFESCI
TITLE:              The relationship between environmental monitoring and
                    biological markers in exposure assessment
AUTHOR:             Rappaport, S.M.; Symanski, E.; Yager, J.W.; Kupper, L.L.
CORPORATE SOURCE:   CB#7400, Univ. North Carolina, Chapel Hill, NC 27599-7400,
                    USA
SOURCE:             HUMAN TISSUE MONITORING AND SPECIMEN BANKING.;ENVIRON.
                    HEALTH PERSPECT., (1995) pp. 49-54;vol. 103, no. 3 suppl.
```

Meeting Info.: Human Tissue Monitoring and Specimen Banking: Opportunities for Exposure Assessment, Risk Assessment, and Epidemiologic Research. Research Triangle Park, NC (USA). 30 Mar-1 Apr 1993.
DOCUMENT TYPE: Journal
TREATMENT CODE: Conference
FILE SEGMENT: X
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The poor quality of traditional assessments of exposure has encouraged epidemiologists to explore biological monitoring in studies of chronic diseases. Yet, despite theoretical advantages, **biomarkers** have not been widely used in such applications. This article compares the general utility of a **biomarker** with that of the measurement of exposure per se. Points are illustrated with a longitudinal study of boat workers in which levels of styrene in the breathing zone and in exhaled air were compared to sister chromatid exchanges (SCEs) in peripheral lymphocytes. First, the linear relationship is explored between personal exposure and the levels of a **biomarker** in the cohort. A good fit to the straight-line relationship reflected by a correlation coefficient which is close to 1, such as observed with styrene in exhaled air (r super(2) = 0.83), suggests linear kinetics, that the appropriate route of exposure was measured by personal monitoring, small interindividual differences, adequate sample sizes, and a specific **biomarker**. However, a small correlation coefficient, as observed between SCEs and styrene exposure (r super(2) = 0.11), indicates that either kinetics were nonlinear or that more complex issues were involved with one or more of these factors. Second, environmental and biologic measurements are compared for use as independent variables in establishing a straight-line relationship between exposure and the health effect. If the ratio of the within-person to the between-person components of variance of the independent variable is large, then significant attenuation results when estimating the slope of the line. Since such attenuation can be reduced by making repeated measurements on each person in the cohort, the **sample sizes required** to reduce the bias to a fixed level can be used to compare the various measures of exposure. Using data from the styrene-exposed workers, it is shown that the slope being estimated would be within 10% of the correct slope parameter with 3 personal measurements of exposure compared to 4 samples of exhaled air (12 measurements) and 20 assays of SCEs. Thus, in this case, the measurement of airborne exposure would be more efficient than that of either exhaled air or SCEs for epidemiologic purposes.